REMARKS

Status of the Claims

Claims 1-51 are currently pending. Claims 1-30 and 43-51 were withdrawn from further consideration in response to a restriction requirement by the Examiner, under 37 C.F.R. §1.142(b).

In the present Response, claims 1-30 and 43-51 are cancelled; claims 31 and 32 are amended; and claim 52 is added. Thus, after entry of these amendments, claims 31-42 and 52 are presented for reconsideration.

Pursuant to the Office Action, claim 32 is rejected under 35 U.S.C. §112, second paragraph. Claims 31, 32, 35, and 42 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 5,491,086 to Gelfand *et al.* (hereinafter "Gelfand"). Claims 31-34 and 36-41 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Gelfand in view of U.S. Patent No. 5,939,250 to Short (hereinafter "Short").

Applicants respectfully traverse all outstanding objections to the specification and objections and rejections of the claims.

Support for the Claim Amendments

Amendments to the specification merely correct typographical errors. Claim 31 has been amended to clarify the scope of the claim. Support for amendments to claim 31 directed to nucleic acid sequences having at least 70% identity to SEQ ID NO:1 can be found, *inter alia,* at page 14, lines 17-24. The method of claim 31 includes nucleic acid sequences of SEQ ID NO:1, nucleic acid sequences having at least 70% identity to SEQ ID NO:1, nucleic acid sequences that are complementary to SEQ ID NO:1 and those having at least 70% identity to SEQ ID NO:1, and fragments that are at least 30 consecutive nucleotides of any of the preceding sequences. Support for the amendment can be found in claim 31, as originally filed. Support for amendments to claim 32 directed to a method which includes gene site saturated mutagenesis

(GSSM) can be found, *inter alia,* at page 32, line 13, to page 33, line 11. Support for new claim 52 directed to variants having polymerase activity can be found, *inter alia,* page 26, line 30, to page 27, line 12. Accordingly, Applicants submit that no new matter has been introduced by the following amendments.

Objections to the Specification

The specification is objected to for having the following informalities:

In the paragraph beginning on page 1, line 1, the Patent Office notes that the term "number" is referred to both as "Number" and "No."

In the paragraph beginning on page 3, line 23, the Patent Office notes that the specification recites "SEQ ID No.:2," whereas all other references to SEQ ID NOs. recite "SEQ ID NO:."

In the paragraph beginning on page 5, line 21, the Patent Office notes that the word "detecting" is indented.

In the paragraph beginning on page 18, line 14, the Patent Office notes that the phrase "in the 5' to 3 sequence" should be "in the 5' to 3' sequence."

Applicants respectfully submit that the instant amendment corrects the informalities. Therefore, this objection can be properly withdrawn.

Issues under 35 U.S.C. §112, first paragraph

Claim 32 is objected to for reciting the method "GSSM" without the full written term to precede it.

Applicants have amended claim 32 to include the full term in the claim. Accordingly, this objection can be properly with withdrawn.

Issues under 35 U.S.C. §112, second paragraph

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as it is alleged that it is unclear what Applicants intend by the recitation "GSSM." Applicants have amended claim 32 to provide the full term and specifically point to pages 32 and 33, where the GSSM technique is described.

Issues under 35 U.S.C. §102

Claims 31, 32, 35, and 42 are rejected under 35 U.S.C. §102(b) as being anticipated by Gelfand. Applicants respectfully traverse this rejection for the reasons set forth below.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention.

The Patent Office alleges that the Gelfand teaches a nucleic acid from *P. occultuim* (SEQ ID NO:3) that is 66.5% identical to instantly disclosed SEQ ID NO:1. The Patent Office further alleges that Gelfand teaches a method for generating a variant of the nucleic acid sequence SEQ ID NO:3 by modifying one or more nucleotides, introduced by oligonucleotide-directed mutagenesis or site-specific mutagenesis.

Applicants have amended claim 31 to recite to methods of generating variants from sequences having at least 70% identity to SEQ ID NO:1. Gelfand does not teach a nucleic acid sequence that is at least 70% identical to SEQ ID NO:1. Accordingly, Gelfand does not teach each and every limitation of amended claim 31. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 31, 32, 35, and 42 based upon 35 U.S.C. §102 as allegedly anticipated by Gelfand

Issues under 35 U.S.C. §103

Claims 31-34 and 36-41 are rejected under 35 U.S.C.§103(a) as allegedly unpatentable over Gelfand in view of Short. Applicants respectfully traverse this rejection for the reasons set forth below.

For a proper rejection under 35 U.S.C. §103(a), the references, either alone or in proper combination, must teach or suggest all the claim limitations of Applicant's claimed invention. Applicant will show that the deficiencies of Gelfand are not cured by Short. Accordingly, a *prima facie* case of obviousness has not been established and the rejection can be properly withdrawn.

As previously states, Gelfand does not teach a nucleic acid sequence that is at least 70% identical to SEQ ID NO:1. Applicants submit that Gelfand also does not suggest a nucleic acid sequence having at least 70% identity to SEQ ID NO:1.

Short is cited to teach a number of techniques for directed mutagenesis that was not taught by Gelfand. Short, however, does not teach or suggest a nucleic acid sequence that is at least 70% identical to SEQ ID NO:1.

Accordingly, neither Gelfand nor Short, alone or in proper combination, teaches or suggests all the claim limitations of the claimed invention. In light of the reasons provided, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 31-34 and 36-41 based upon 35 U.S.C. §103 as allegedly unpatentable over Gelfand in view of Short.

CONCLUSION

Claims 1-51 are pending in the instant application. Claims 1-30 and 43-51 have been cancelled; claims 31 and 32 have been amended; and claim 52 has been added by the instant Response. Applicants request that the Examiner reconsider the application and claims in light of

the foregoing reasons and amendments and respectfully submit that the claims are in condition for allowance.

If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity to discuss any outstanding issues and to work with the Examiner toward placing the application in condition for allowance.

Attached is a marked-up version of the changes being made by the current amendment.

Applicants believe that no fees are necessitated by the present Response. However, in the event any fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

Respectfully submitted,

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Version with markings to show changes made

In the specification:

Paragraph beginning at page 1, line 1 has been amended as follows:

This application is a Continuation-in-Part application of co-pending U.S. Patent Application Serial No. [Number] 09/391,340, filed September 7, 1999, which is a divisional of U.S. Patent Application Serial No. 08/907,166, filed August 6, 1997, now issued as U. S. Patent No. 5,948,666.

Paragraph beginning at page 3, line 23 has been amended as follows:

Another aspect of the invention is an isolated nucleic acid encoding a polypeptide or a functional fragment thereof having a sequence as set forth in SEQ ID NO:2 [No: 2,] and sequences substantially identical thereto.

Paragraph beginning at page 5, line 21 has been amended as follows:

Another aspect of the invention is an assay for identifying fragments or variants of SEQ ID NO: 2, and sequences substantially identical thereto, [and sequences substantially identical thereto,] which retain the extreme high temperature polymerase activity of the polypeptides of SEQ ID NO: 2 (i.e., at temperatures of 95°C to 113° C, for four or more hours. The assay includes utilizing a polypeptide encoded by a nucleic acid having at least 70% homology to SEQ ID NO: 1, and sequences substantially identical thereto, or polypeptide fragment or variant encoded by SEQ ID NO: 1, to effect DNA polymerase activity in a PCR amplification at extreme high temperature for four or more hours and under conditions that allow said polypeptide or fragment or variant to function, and [paragraph and indent]

detecting formation of an amplification product, wherein formation of the amplification product is indicative of a functional DNA polymerase polypeptide or fragment or variant.

Paragraph beginning at page 18, line 14 has been amended as follows:

In [a] one embodiment, the ligation reassembly process is performed exhaustively in order to generate an exhaustive library. In other words, all possible ordered combinations of the nucleic acid building blocks are represented in the set of finalized chimeric nucleic acid molecules. At the same time, the assembly order (i.e. the order of assembly of each building block in the 5' to 3' [3] sequence of each finalized chimeric nucleic acid) in each combination is by design (or non-stochastic). Because of the non-stochastic nature of the method, the possibility of unwanted side products is greatly reduced.

Paragraph beginning at page 26, line 30 has been amended as follows:

Therefore, in [a] one embodiment, the invention relates to a method for producing a biologically active hybrid polypeptide and screening such a polypeptide for enhanced activity by:

1) introducing at least a first polynucleotide in operable linkage and a second polynucleotide in operable linkage, said at least first polynucleotide and second polynucleotide sharing at least one region of partial sequence homology, into a suitable host cell;
2) growing the host cell under conditions which promote sequence reorganization resulting in a hybrid polynucleotide in operable linkage;
3) expressing a hybrid polypeptide encoded by the hybrid polynucleotide;
4) screening the hybrid polypeptide under conditions which promote identification of enhanced biological activity; and
5) isolating the [a] polynucleotide encoding the hybrid polypeptide.

In the claims:

Claims 1-30 and 43-51 have been cancelled

Claims 31 and 32 have been amended as follows:

31. (Amended) A method of generating a variant comprising:

obtaining a nucleic acid comprising a sequence as set forth in SEQ ID NO:1, sequences having at least 70% identity [substantially identical] thereto, sequences complementary to SEQ ID NO:1 or sequences having at least 70% identity to SEQ ID NO:1 [thereto], and fragments comprising at least 30 consecutive nucleotides thereof, [and fragments comprising at least 30 consecutive nucleotides of the sequences complementary to SEQ ID NO:1] and

modifying one or more nucleotides in said sequence to another nucleotide, deleting one or more nucleotides in said sequence, or adding one or more nucleotides to said sequence.

32. (Amended) The method of claim31, wherein the modifications are introduced by a method selected from the group consisting of error-prone PCR, shuffling, oligonucleotide-directed mutagenesis, assembly PCR, sexual PCR mutagenesis, *in vivo* mutagenesis, cassette mutagenesis, recursive ensemble mutagenesis, exponential ensemble mutagenesis, site-specific mutagenesis, ligation reassembly, gene site saturated mutagenesis (GSSM) [GSSM] and any combination thereof.

Claim 52 has been added.